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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/683,990	10/10/2003	James McSwiggen	MBHB04-736 (400/134)	3438

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1633	
MAIL DATE	**DELIVERY MODE**
08/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/683,990	MCSWIGGEN ET AL.	
	Examiner	**Art Unit**	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6-08-07.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,13-21,30,33 and 37-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,13-21,30,33 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1, 3, 13-21, 30, 33, and 37-39 are presently pending.

3. Applicant's arguments with respect to the rejection of claims 1, 3, 13-21, 30 and 33, under 35 USC 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Response to Arguments

Claim Rejections - 35 USC § 103

4. Claims 1 3, 13-21, 30, 33, and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carmeliet et al. (WO 01/85796 A2), in view of GenBank Accession No. NM_002632, Parrish et al. (Molecular Cell 2000, vol. 6, pages 1077-1087), and Agrawal et al. (WO 9401550 A1)

The teachings of Carmeliet et al. aims to provide research tools for the study of pathological angiogenesis. In one particular embodiment, this invention aims at providing antagonist of placental growth factor (PGF): see page 8, lines 1-14 of this reference:

Also within the scope of the invention are oligoribonucleotide sequences, that include anti-sense RNA and DNA molecules and ribozymes that function to inhibit the translation of VEGFR-1 mRNA or PIGF mRNA. Anti-sense RNA and DNA molecules act to directly block the translation of mRNA by binding to targeted mRNA and preventing protein translation. In regard to antisense DNA, oligodeoxyribonucleotides derived from the translation initiation site, e.g., between -10 and +10 regions of the VEGFR-1 or PIGF nucleotide sequence, are preferred. Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. The mechanism of ribozyme action involves sequence specific hybridization of the ribozyme molecule to complementary target RNA, followed by a endonucleolytic cleavage. Within the scope of the invention are engineered hammerhead motif ribozyme molecules that specifically and efficiently catalyze endonucleolytic cleavage of VEGFR-1 or PIGF RNA sequences.

However, Carmeliet et al. does not disclose the specific nucleotide sequence encoding human placental growth factor 1 of SEQ ID NO: 257, as recited in the instant claims, nor does it particularly disclose the use of double stranded nucleic acid having the particular modifications recited in the instant claims.

The sequence of human placental growth factor 1 set forth in SEQ ID NO: 257 was previously disclosed in GenBank Accession No. NM_002632.

Elbashir et al. teach that RNA interference is mediated efficiently by chemically synthesized RNAs that are 21-23 nucleotides in length and name these short duplexes "short interfering RNAs" (siRNAs). These siRNAs are formulated into compositions with a pharmaceutically acceptable carrier for transfection into cells. Elbashir et al. also teach that siRNAs containing nucleotide modifications known in the art such as 2'-OMe substitutions can stimulate RNA interference. Parrish et al. teach that some common nucleotide modifications, including sugar modifications such as 2'-fluoro, base modifications such as 5-modified uridines and phosphorothioate backbones are tolerated in interfering RNAs.

Agrawal et al. teaches self-stabilized oligonucleotides where the self-stabilized oligonucleotide comprises an antisense portion and a self-complementary portion. It is taught that these oligonucleotides form a completely or partially double-stranded structure (see page 5, for example). It is taught at page 8, for example, that the oligonucleotides of their invention includes such molecules containing modified nucleic acid bases and/or sugars. At page 10 it has been taught that the antisense portion can be from about 8 to 50 nucleotides in length. At page 13 it has been taught that the oligonucleotides can be RNA, DNA, or combinations thereof. At pages 14 and 16 it has been taught various internucleotide linkages that can be used in their invention. At page 15 it has been taught, for example, that the double stranded region can be fifty nucleotides or less. At pages 15-16 it has been taught linkers that may be used to join separate antisense and self-complementary strands, for example. At column 16 it is also taught to hyperstabilize the self-stabilized oligonucleotides with 2'-O-me-ribonucleotides. At page 2, it has been taught that 3' caps were known in the art to reduce endonuclease activity. Agrawal also teaches pharmaceutical carriers for the delivery of their invention. The Agrawal invention is drawn to self-stabilized oligonucleotides that are used in antisense methods.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the cited references to make double stranded nucleic acid molecules capable of down-regulating the placental growth factor-1 gene (PGF-1). Carmeliet et al. teach the use of nucleic acid based inhibitors, including antisense DNA and RNA as a means to antagonize the activity of PGF-1. Elbashir et al. provide a motivation to make and design double stranded nucleic acid inhibitors to inhibit the expression of a target gene. Parrish et al. provide a motivation to use double stranded nucleic acid containing modified sugar, base and backbone modifications, teaching that such modifications, which are well-known and routinely used in the antisense field, are tolerated in RNA interference. One of ordinary skill in the art would have had a reasonable expectation of success in making double stranded nucleic acid to down-regulate the expression of the PGF-1 gene because Carmeliet et al. teach that PGF-1 gene expression can be inhibited by the activity of RNA inhibitors, and Elbashir et al. and Parrish et al. teach the feasibility of designing a dsRNA molecule to inhibit the activity of a target gene having a known nucleotide sequence (see GenBank Accession No. NM_002632). One of ordinary skill in the art would have had a reasonable expectation of success in making double stranded nucleic acid having sugar, base and backbone modifications because Elbashir et al. and Parrish et al. each teach that interfering RNAs containing such modifications are active in provoking RNA interference. Furthermore, Agrawal et al. clearly teach that stabilized nucleic acid, DNA or RNA, comprising modifications and a double stranded structure was effective in inhibiting the expression of a target gene.

Moreover, it would have been obvious to modify the teachings of the cited references to design siRNA molecules targeting human placental growth factor 1 of

SEQ ID NO: 257, and further comprising the various modifications described by Parrish et al., Elbashir et al., and Agrawal et al. since these references provide teachings to guide the ordinary skilled artisan to modify the siRNA molecule to comprise 2'-O-methyl modifications, 2'-fluoro modifications, for the purpose of increasing nuclease resistance, without the loss of RNAi activity.

Double Patenting

5. Claims 1 3, 13-21, 30, 33, and 37-39 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-35 of copending Application No. 10/922,761. Applicants stated that they would file a terminal disclaimer at the appropriate time. However, Applicants did not provide any arguments to address the merits of the rejection therefore, the instant claims remain rejected for the reasons of record.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE